Claims

1. An antibody molecule capable of specifically recognizing two regions of the β-A4 peptide/Aβ4, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof.

2. The antibody molecule of claim 1, wherein said antibody molecule recognizes at least two consecutive amino acids within the two regions of β-A4.

3. The antibody molecule of claim 1 or 2, wherein said antibody molecule recognizes in the first region an amino acid sequence comprising: AEFRHD, EF, EFR, FR, EFRHDSG, EFRHD or HDSG and in the second region an amino acid sequence comprising: HHQKL, LV, LVFFAE, VFFAED or VFFA, FFAEDV.

4. The antibody molecule of any one of claims 1 to 3, wherein said antibody molecule comprises a variable V_H-region as encoded by a nucleic acid molecule as shown in a SEQ ID NO selected from the group consisting of SEQ ID NO: 3, 5 or 7 or a variable V_H-region as shown in a SEQ ID NO: selected from the group consisting of SEQ ID NOs: 4, 6 and 8.

5. The antibody molecule of any one of claims 1 to 3, wherein said antibody molecule comprises a variable V_L-region as encoded by a nucleic acid molecule as shown in a SEQ ID NO selected from the group consisting of SEQ ID NO: 9, 11 and 13 or a variable V_L-region as shown in a SEQ ID NO selected from the group consisting of SEQ ID NOs: 10, 12 and 14.

6. The antibody molecule of any one of claims 1 to 5, wherein said antibody molecule comprises at least one CDR3 of an V_L-region as encoded by a nucleic acid molecule as shown in SEQ ID NOs: 15, 17 or 19 or at least one CDR3 amino acid sequence of an V_L-region as shown in SEQ ID NOs: 16, 18 or 20 and/or wherein said antibody molecule comprises at least one CDR3 of an V_H-region as encoded by a nucleic acid molecule as shown in SEQ ID NOs: 21, 23 or 25 or at least one CDR3 amino acid sequence of an V_H-region as shown in SEQ ID NOs: 22, 24 or 26.

7. The antibody molecule of any one of claims 1 to 6, wherein said antibody is selected from the group consisting of MSR-3, -7 and -8 or an affinity-matured version of MSR-3, -7 or -8.

8. The antibody molecule of any one of claims 1 to 7, wherein said antibody molecule is a full antibody (immunoglobulin), a F(ab)-fragment, a $F(ab)_2$-fragment, a single-chain antibody, a chimeric antibody, a CDR-grafted antibody, a bivalent antibody-construct, a synthetic antibody or a cross-cloned antibody.

9. The antibody molecule of any one of claims 1 to 8, wherein said at least two regions of β-A4 form a conformational epitope or a discontinuous epitope.

10. The antibody molecule of claim 8 or 9, wherein said cross-cloned antibody is selected from the group consisting of
MS-R #3.3H1x3.4L9;
MS-R #3.6H5 x 3.6L2;
MS-R #3.6H8 x 3.6L2;
MS-R #7.4H2 x 7.2L1;
MS-R #7.9H2 x 7.12L2;
MS-R #7.9H4 x 7.12L2;
MS-R #7.11H1 x 7.11L1;
MS-R #7.11H1 x 7.2L1;
MS-R #3.4H1 x 3.4L9;

MS-R #3.4H3 x 3.4L7;
MS-R #3.4H3 x 3.4L9;
MS-R #3.4H7 x 3.4L9;
MS-R #3.4H7 x 3.4L7;
MS-R #3.6H5 x 3.6L1;
MS-R #7.2H2 x 7.2L1;
MS-R #7.4H2 x 7.12L2;
MS-R #7.9H2 x 7.2L1;
MS-R #7.9H2 x 7.12L1;
MS-R #7.11H2 x 7.2L1;
MS-R #7.11H2 x 7.9L1;
MS-R #7.11H2 x 7.12L1 or
MS-R #8.1H1 x 8.2L1.

11. A nucleic acid molecule encoding an antibody molecule of any one of claims 1 to 10.

12. A vector comprising the nucleic acid molecule of claim 11.

13. A host cell comprising the vector of claim 12.

14. A method for the preparation of an antibody molecule of any one of claims 1 to 10 comprising culturing the host cell of claim 13 under conditions that allow synthesis of said antibody molecule and recovering said antibody molecule from said culture.

15. A composition comprising an antibody molecule of any one of claims 1 to 10 or an antibody molecule produced by the method of claim 14.

16. The composition of claim 15, which is a pharmaceutical or a diagnostic composition.

17. Use of an antibody molecule of any one of claims 1 to 10 or an antibody molecule produced by the method of claim 14, of a nucleic acid molecule of claim 11, of a vector of claim 12 or a host of claim 13 for the preparation of a pharmaceutical composition for the prevention and/or treatment of a disease associated with amyloidogenesis and/or amyloid-plaque formation.

18. Use of an antibody molecule of any one of claims 1 to 10 or an antibody molecule produced by the method of claim 14 for the preparation of a diagnostic composition for the detection of a disease associated with amyloidogenesis and/or amyloid-plaque formation.

19. Use of an antibody molecule of any one of claims 1 to 10 or an antibody molecule produced by the method of claim 14 for the preparation of a pharmaceutical composition for the disintegration of β-amyloid plaques.

20. Use of an antibody molecule of any one of claims 1 to 10 or an antibody molecule produced by the method of claim 14 for the preparation of a pharmaceutical composition for passive immunization against β-amyloid plaque formation.

21. The use of claims 17 or 18, wherein said disease is dementia, Alzheimer's disease, motor neuropathy, Down's syndrome, Creutzfeld Jacob disease, hereditary cerebralhemorrhage with amyloidosis Dutch type, Parkinson's disease, HIV-related dementia, ALS or neuronal disorders related to aging.

22. Kit comprising an antibody molecule of any one of claims 1 to 10, a nucleic acid molecule of claim 16, a vector of claim 17 or a host cell of claim 18.

23. A method for the optimization of an antibody molecule as defined in any one of claims 1 to 10 comprising the steps of

(a) constructing a library of diversified Fab antibody fragments derived from an antibody comprising at least one CDR3 of an V_H-region as encoded by a nucleic acid molecule as shown in SEQ ID NOs: 21,23 or

25 or at least one CDR3 amino acid sequence of an V_H-region as shown in SEQ ID NOs: 22, 24 or 26;

(b) testing the resulting Fab optimization library by panning against Aβ/Aβ4;

(c) identifying optimized clones; and

(d) expressing of selected, optimized clones.

24. The method of claim 23 further comprising a step (ca), whereby the optimized clones are further optimized by cassette mutagenesis

25. The method of claim 23 or 24, wherein said Aβ/Aβ4 in step (b) is aggregated Aβ/Aβ4.

26. The method of any one of claims 23 to 25, wherein said identification in step (c) is carried out by koff-ranking.

27. A method for the preparation of a pharmaceutical composition comprising the steps of

(a) optimization of an antibody according to the method of any one of claims 23 to 26; and

(b) formulating the optimized antibody/antibody molecule with an physiologically acceptable carrier.

28. A pharmaceutical composition prepared by the method of claim 27.